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13. ABSTRACT (Maximum 200 words) <p>An increase in breast cancer incidence among younger women has been observed; thus, many young breast cancer patients are faced with questions concerning their reproductive futures. At present it is unclear whether attempting childbearing may increase these women's risk of death. This project obtained data from three population-based cancer registries in the Seattle, Detroit, and Los Angeles areas to compare relative survival of women with and without births among those with breast cancer. All women less than 45 years of age diagnosed with invasive breast cancer were identified in each of the three study regions. Their records were linked with birth certificates from each state to identify those (3%) with a live birth after their initial diagnosis with breast cancer. Comparison subjects were identified from among young women with breast cancer in each region without subsequent births, matched on age and stage of disease at diagnosis, diagnosis year, race, and presence of multiple primary tumor. Date of last follow-up and vital status have been updated and 75% of all study subjects who were known to be alive have been followed for at least four years. Relative survival will be compared among women with and without births subsequent to diagnosis.</p>				
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FOREWORD

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I. INTRODUCTION

The nature of the problem and the study objectives have not changed over the previous year and are restated below. The review of previous work has been abbreviated similarly to last year's report, and only includes results of studies reported during the last year. A more comprehensive review of the literature is contained in the 1996 annual report.

I.A. Nature of the problem (Summary of Subject and Purpose of Research)

The incidence of breast cancer among women less than 45 years of age is increasing, and young women appear to have relatively poor survival [White 1987; Ranstam 1990]. The prognosis may be even worse for women who are pregnant at diagnosis; however, the effect on survival is unknown. As the increase in breast cancer incidence among younger women coincides with a trend towards delayed childbearing, information regarding the association of subsequent pregnancy and survival is needed so that women with breast cancer and their physicians can make informed choices concerning family planning.

At present there is no general consensus among physicians providing care to young women with breast cancer about how to advise them regarding their future reproduction [Saunders 1993]. Current clinical recommendations concerning a waiting period of 2–3 years (the peak period of recurrence) after the conclusion of breast cancer treatment before attempting pregnancy are based on psychosocial and moral issues rather than scientific studies linking pregnancy with poorer survival [vanderVange 1991; Saunders 1993]. Young women who survive their initial breast cancer treatment are justifiably confused concerning their reproductive future.

I.B. Recent related research by other investigators (Background of Previous Work Since the 1997 Progress Report)

Since the literature search conducted in 1997, only two more studies were identified that evaluated recurrence or survival associated with pregnancy or childbearing after breast cancer diagnosis. In a population-based study conducted in Denmark [Kroman 1997], the investigators observed a nonsignificant reduced risk of death (RR: 0.55, 95% CI: 0.28–1.06) among women who had a full-term pregnancy after breast cancer treatment, as compared to women who did not. This trend toward a decreased risk was still evident after adjustment for age at diagnosis, stage of disease, and reproductive history before diagnosis. However, in a separate case-control study [Bonnier 1997], the investigators concluded that, similar to other studies that evaluated women with pregnancy-associated breast cancer, pregnancy at the time of diagnosis has an adverse effect on the outcome of breast cancer. This provides further justification for analyzing women with births occurring ten or more months after diagnosis separately from those with births occurring soon after diagnosis. A recent review article evaluating the effect of pregnancy after breast cancer concluded that “pregnancy does not increase the risk of recurrent breast cancer” [Collichio 1998], a conclusion largely based on studies reported through 1996. In summary, although it appears more evident that women who are pregnant at diagnosis are more likely to experience decreased survival relative to women who are not, the evidence for an association between survival and pregnancy or childbirth after diagnosis remains unclear.

II. BODY OF PROGRESS REPORT (Including a Summary of Experimental Methods and Procedures)

II.A. Study tasks completed

The study activities proposed in the revised statement of work that have been completed are listed below:

Task 1: Identification of exposed cohorts and protocol development – Women <45 years of age at first diagnosis of invasive breast cancer during the years 1980 – 1993 were identified from central cancer registries in the Seattle, Detroit, and Los Angeles areas. This included 3,925 from Seattle; 4,496 from Detroit, and 6,962 from Los Angeles. Data tapes containing birth certificate information from 1980 – 1994 from Washington and Michigan and from 1980 – 1993 in California were obtained from each respective State Department of Health. A computer algorithm to link cancer registry data with birth certificate data was developed in Seattle to match birth records of infants in each state born to study subjects after their breast cancer diagnosis. This program was provided to each of the other study regions so that similar criteria were used in conducting linkages at each site. In all regions, data for women with breast cancer diagnosed during one calendar year were linked to birth certificates for the period of time including the same calendar year and all subsequent years of the study period. However, if a woman was known to be deceased, birth certificates for the years after her death were not searched. Validity of the linkage protocol was documented for the Seattle data using interviews obtained on a portion of the study subjects (~400) and was described in the previous year's report.

Task 2: Identification and refinement of unexposed cohorts – A preliminary matching program was developed in Seattle for identification of the comparison women. The first version of the program included the following matching criteria: age at diagnosis (exact match, within one year, within two years); year of diagnosis (1980-84, 1985-89, 1990+); stage of disease at diagnosis (exact match); and race (exact match).

Since the matching was conducted within each region, exposed and comparison women were also matched on region. The potential pool of comparison candidates (essentially all women <45 years of age diagnosed during the same time period but without a subsequent birth identified in the birth certificates) was first stratified into groups based on the matching criteria and a variable designating the matching group identity was created. Based on these same criteria, a matching group identity variable was also calculated for each exposed woman and then each exposed woman was allowed to draw as many comparison subjects as possible from the potential pool of candidates within the same matching group. The preliminary matching program was run in Seattle and was made available to the other sites. The data files resulting from this first version of the program were used in the preliminary results reported in the abstracts required by the Department of Defense (DOD) in May 1997.

The results of the matching program were subsequently discussed in a teleconference in March 1997 with the investigators as described in the last progress report. To avoid a "healthy mother" bias and to ensure that exposed women were matched to unexposed women with similar health status, the matching program was refined so that women who had been diagnosed prior to their diagnosis of breast cancer with other, non-breast primary tumors would also be matched to women with similar, non-breast primary tumors diagnosed during the same interval. Women who had been diagnosed with another primary tumor during the interval between breast cancer diagnosis and the date of birth of their child (or the reference date for unexposed women) would be excluded. Having another primary tumor occur after reference date, however, was not included as a matching variable, nor was it a basis for exclusion from the study. The occurrence of this will, however, be described in both groups and evaluated for its effect on outcome. The matching program was also revised to allow all unexposed subjects within a stratum equal probability of being selected as a match for an exposed subject within the same stratum. Data resulting from the second version of the matching program were used to produce the annual report provided for the DOD in August 1997. These data were also used to create the poster presented at the DOD's Era of Hope Conference in October 1997.

A third refinement of the matching program was distributed to all study centers in October 1997. Because of the strict matching criteria, a small number of cases were without any controls after running the program. For this reason, a protocol to conduct manual matches was developed in Seattle and made available to the other regions in November 1997. This protocol employed the matching criteria defined in the program, but allowed study coordinators in each of the regions to relax these criteria using investigator-approved guidelines (e.g., relaxing year of diagnosis by one year) so that at least one control could be found for each of these unusual cases. The results from the manual matching process were discussed in a teleconference on February 20, 1998 attended by Dr. Beth Mueller (PI, Seattle), Ms. Aruna Kamineni (Study Coordinator, Seattle), Dr. Michael Simon (PI, Detroit), Mr. Asim Khan (Study Coordinator, Detroit), Dr. Dennis Deapen (PI, Los Angeles), Ms. Frances Wang (Programmer, Los Angeles), and Dr. Ann Hamilton (Biostatistician, Los Angeles). The characteristics of the hard-to-match cases were evaluated and the potential choices selected by each of the regions were discussed and approved. Hand-matched controls (n=39) were flagged so that separate analyses could be conducted in which they were excluded in order to determine whether this procedure had any measurable effect on results.

Task 3: Follow-up subjects to ascertain survival status and protocol development – After the comparison cohort of women without births was identified, follow-up for each study region continued through March 1998. At all registries, routine periodic linkages with death certificates for each state are conducted. In Los Angeles, the registry conducted active follow-up on all potential subjects in their region via credit bureau searches. In Seattle, subjects who had agreed to participate in other research studies after their diagnosis were identified and additional follow-up information was obtained from these studies, to be used in site-specific analyses with data from Seattle only.

II.B. Remaining study tasks in progress and planned

In March 1998, Dr. Beth Mueller (PI, Seattle) requested a one-year no-cost extension for this project to reflect a more appropriate allotment of time and effort given the progress of the project. Since the project involves multi-step data linkages conducted separately in three states followed by creation of a single data file for analyses to be conducted in Seattle, the necessary data editing activities prior to statistical analysis took longer than anticipated at each of the local study centers. The request was approved in May 1998 (Modification P80001 for Grant No: DAMD17-94-J-4262) and the time/effort of the Study Coordinator in Seattle, Ms. Kamineni, was re-allocated to reflect a somewhat lower level of her time and effort during site-specific data editing, with a greater level to be utilized during the statistical analyses and preparation of the final report. Ms. Kamineni has coordinated the site-specific activities as necessary during this time, and is now again more involved in direct data handling since these activities were completed.

Task 4: Obtain data for subset analysis from Seattle – Separate research studies at the Fred Hutchinson Cancer Research Center that included young women with invasive breast cancer were identified. Ms. Kamineni has obtained the necessary data to create a subfile of Seattle area data only, containing additional variables including information pertaining to other factors potentially related to breast cancer survival (e.g., use of oral contraceptives, body mass index, reproductive history, family history, etc.). The subjects in the present study who were also involved in these other research activities have been identified and Ms. Kamineni is currently working to uniformly merge the appropriate variables from the various data files so that analysis on this subset of women can begin.

Task 5: Data editing, analysis and manuscript preparation – Many aspects of data editing have been in progress since the study began. This includes creation of a uniform data dictionary for registry and birth certificate data from all sites, a coding guide, and examination of preliminary data obtained at each phase of the study. Data from all three sites have been merged into an analysis file to evaluate survival relative to childbirth. Further editing of the merged files is necessary to create uniform birth certificate variables in order to create an analysis file containing these variables. Preliminary analysis of the combined data has started. Updated literature searches have been performed periodically and will be repeated prior to submission of manuscripts to scientific journals.

III. RESULTS TO DATE (Conclusions)

III.A. Result of data linkages

The number of women, <45 years of age, with invasive breast cancer identified in each region during the study period included 3,925 in the Seattle area, 4,496 in Detroit, and 6,962 in Los Angeles (Table 1). Because data for 1994 were also available at the time the linkage was conducted in Seattle, this year was also included in the linkage for that site at no additional cost. Birth certificate records for 1980 – 1993 were obtained in each state. Due to the nature of the existing agreements between the Cancer Registries and the Department of Health in Seattle and Detroit, access to an additional year of birth certificate data was also possible, and data from

1994 birth certificates was used in conducting the linkages at no extra cost. This was done to increase the number of exposed subjects (those with births after diagnosis) with a resultant increase in statistical power. In Los Angeles, the linkages were conducted beginning with the most recent years of data. When data for 1980 – 1981 were examined, it was discovered that the birth certificates for California do not contain the mothers' names or any other identifier (e.g., Social Security Number) that could be used to link data. For this reason, it was not possible to link registry data to these two early years of follow-up in the Los Angeles region. As relatively few linkages were identified in these early years of follow-up at the other two sites, it is possible, however, that few linkages were missed as a result of this. The possibility of misclassification of women with early births as unexposed women, however, will be considered in interpreting results. As the proposed method of analysis (Cox proportional hazards regression) relies on person-time of follow-up with left censoring occurring at the subject's date of childbirth, use of slightly different years of diagnosis and follow-up for the subjects at different study sites should have no impact on the analysis.

The number of women with births identified in the birth certificates includes 104 in Seattle; 120 in Detroit; and 228 in Los Angeles, representing approximately 3% of the total women with breast cancer. This proportion is slightly lower than that predicted based on the preliminary linkage conducted in Seattle prior to this project and is the result of several factors. First, the preliminary linkage was conducted as an unfunded activity without any refinement and included all possible linkages as a result of the file merge. In the present study, criteria were established to refine the accuracy of the linkage and several potential linkages were reviewed and discarded as inaccurate. Second, in the preliminary linkage a woman with multiple primary tumors may have had more than one registry record, inflating the number of birth record linkages. In the present study, programming resources were available to eliminate these "duplicate" records prior to linkage. Finally, linkages were further refined in the present study based on dates of the birth (on the birth certificate) and dates of diagnosis (from the Registry). Since a year of Registry data was linked to that same year and subsequent years of birth certificate data, some of the resultant linkages represent births that occurred during the same year, but prior to the breast cancer diagnosis. These linkages were excluded. Because of previous evidence that survival among women with pregnancy-associated breast cancer diagnosis (diagnoses made while pregnant) is lower than among those with non-pregnancy-associated breast cancer diagnoses [Lethaby 1996; Anderson 1996], data will be analyzed for these groups separately.

III.B. Characteristics of women with subsequent births at each site

The mean age of breast cancer patients in all study regions who subsequently gave birth was approximately 32 years of age (Table 2). Nearly half of these women were diagnosed with invasive breast cancer during the years 1985 – 1989, and 56% – 63% had local stage disease at diagnosis, with approximately another third diagnosed with regional disease. Relatively few (ranging from 2% in Seattle to 5% in Los Angeles) had distant stage disease. Approximately 16% of subjects in all regions were Black (4% in Seattle; 33% in Detroit; 12% in Los Angeles), and 5% were of Asian ethnic groups or countries of origin (Japanese, Chinese, Filipino, Korean, and Vietnamese).

Previous studies have demonstrated significantly worse survival among women who were pregnant at diagnosis. For this reason, separate analyses will be conducted for these women and for those whose pregnancies began after their diagnosis. 109/452 (24%) of study subjects gave birth <10 months after their diagnoses, indicating that they were pregnant at the time of diagnosis (Figure 1). 343/452 (76%) had births 10 months or longer after their breast cancer diagnoses (Figure 2).

III.C. Characteristics of women with and without births ≥ 10 months after diagnosis identified in birth certificates

Initial analyses will be restricted to only those women (and their comparison subjects) who gave birth at least 10 months after diagnosis. This is to remove the effects of pregnancy-related cancer (which has previously been demonstrated to have relatively poor survival) and because comparison subjects were less readily available for the entire group as a whole. A mean of 5 comparison subjects were identified for each woman with a birth occurring ≥ 10 months after diagnosis, with a maximum of 12 comparison subjects per exposed woman.

Characteristics of women with births ≥ 10 months after diagnosis and their matched comparison subjects without births identified in the birth certificates in each region are shown in Tables 3a – 3c. Because of the variable number of comparison subjects per exposed woman, and because the data are presented categorically for all variables shown (whereas the matching program did not select subjects within categories for all variables), a strict correspondence between the proportions of subjects within each matching category for exposed and unexposed women would not be expected.

Women in each region were generally similar with respect to age at breast cancer diagnosis, with approximately 38% – 50% being between 30 – 34 years of age at diagnosis. About 60% – 67% had local stage disease at diagnosis. Only one exposed woman had had a previous primary cancer (non-breast); two comparison women without births were identified who had also had a prior primary cancer. Five exposed women were also identified who had had a non-breast primary during the interval between their breast cancer diagnosis and when they gave birth. 29 comparison women were identified who also had subsequent primaries occurring before reference date. Consistent with the variations in the base populations in each region, the proportions of African Americans in each exposed group were 5% (Seattle), 32% (Detroit), and 14% (Los Angeles). The proportions of Asian American women with subsequent births were 2% (Seattle), 0% (Detroit) and 8% (Los Angeles). Although the proportion of women known to be alive at last follow-up was consistently higher for those with births than for those without births in each region, these figures are not adjusted for important confounding factors and should not be used to measure relative survival, but are included to provide interim results at this time.

III.D. Results of follow-up of subjects

At the most recent follow-up from each registry, a slightly greater proportion of women with subsequent births ≥ 10 months after diagnosis were alive at follow-up (81%) than of women without subsequent births (74%). The extent of follow-up available for subjects who were alive at their most recent follow-up is reported in Table 4. The percent of subjects for whom no additional follow-up was available after their diagnosis date ranged from 0.2% (unexposed women in Seattle) to 4.9% (unexposed women in LA). Since these subjects will not contribute survival information to the Cox proportional hazards regression model, they will be excluded from the analysis. At least 85% of the subjects from all study regions were followed-up for more than five years after their breast cancer diagnosis.

Estimates of the relative risk of dying and 95% confidence intervals associated with a woman's status concerning the occurrence of births subsequent to breast cancer diagnosis will be derived using Cox proportional hazards regression. This will be conducted using the STATA statistical package. In these analyses, age of diagnosis will be controlled for as a continuous variable. Stage of disease at diagnosis, race/ethnicity, year of diagnosis, and presence of prior multiple primary tumors (the matching variables) will also be controlled. Cumulative survival of women with and without births will be measured with left truncation of survival times at the reference date (date of birth or same date for matched comparison subjects) since women were required to be alive at this point to be eligible for the study. Thus, we will compute the risk of dying associated with having a subsequent birth among women who had similar periods of survival after diagnosis, conditional on their having survived until reference date after diagnosis. Observations will be right censored at either the date of most recent follow-up or date of death. This technique has been used previously in similar studies [Malone 1996].

Table 1. Number of women (< 45 years) with a first, invasive breast cancer, and proportion with subsequent births identified through birth certificates by region

	Seattle	Detroit	Los Angeles	All Regions
Years of diagnosis	1980-1994	1980-1993	1980-1993	1980-1994
No. of women with breast cancer	3925	4496	6962	15,383
Years of birth records searched	1980-1994	1980-1994	1982-1993	1980-1994
No. of women with births identified through birth certificates				
<i>total births identified</i>	104 (3%)	120 (3%)	228 (3%)	452 (3%)
<i>birth <10 months after dx</i>	22	30	57	109
<i>birth ≥10 months after dx</i>	82	90	171	343

Table 2. Demographic and disease characteristics of breast cancer cases with births after diagnosis

	Seattle		Detroit		Los Angeles		All Regions	
	n=104		n=120		n=228		n=452	
mean age (\pm SE) at diagnosis (years)	31.8 \pm 4.1		31.1 \pm 4.7		32.3 \pm 4.0		31.9 \pm 4.3	
diagnosis year	<u>n</u>	<u>%</u>	<u>n</u>	<u>%</u>	<u>n</u>	<u>%</u>	<u>n</u>	<u>%</u>
80-84	30	28.9	36	30.0	78	34.2	144	31.9
85-89	45	43.3	52	43.3	111	18.7	208	46.0
90-94	29	27.9	32	26.7	39	17.1	100	22.1
stage								
local	65	62.5	73	60.8	128	56.1	266	58.9
regional	26	34.6	42	35.0	77	33.8	155	34.3
distant	2	1.9	2	1.7	11	4.8	15	3.3
unknown	1	1.0	3	2.5	12	5.3	16	3.5
race/ethnicity								
white	95	91.4	79	65.8	164	71.9	338	74.8
black	4	3.9	40	33.3	28	12.3	72	15.9
Asian	4	3.8	1	0.8	20	7.5	22	4.9
other	0	0.0	0	0.0	13	5.7	13	2.9
unknown	1	1.0	0	0.0	6	2.6	7	1.6

Table 3a. Characteristics of women in the Seattle area with primary breast cancer diagnosed 1980-94 who have and have not given birth ≥ 10 months after diagnosis

	Women w/ birth ≥ 10 months after diagnosis			
	women w/ birth (cases) n=82		women w/o birth (matched controls) n=544	
	n	%	n	%
age at diagnosis				
<25	3	3.7	3	0.6
25-29	24	29.3	58	10.7
30-34	38	46.3	286	52.6
35-39	15	18.3	171	31.4
40-44	2	2.4	26	4.8
diagnosis year				
80-84	26	31.7	164	30.2
85-89	37	45.1	240	44.1
90-94	19	23.2	140	25.7
stage				
local	55	67.1	357	65.6
regional	26	31.7	185	34.0
distant	0	0.0	0	0.0
unknown	1	1.2	2	0.4
race				
white	76	92.7	531	97.6
black	4	4.9	10	1.8
Asian	2	2.4	3	0.6
other	0	0.0	0	0.0
unknown	0	0.0	0	0.0
multiple primaries				
none or after dx and after cases' birth	81	98.8	541	99.5
before birth and before dx	0	0.0	0	0.0
after dx but before cases' birth	1	1.2	3	0.6
vital status at follow up				
alive	70	85.4	421	77.4
dead	12	14.6	123	22.6

Table 3b. Characteristics of women in the Detroit area with primary breast cancer diagnosed 1980-93 who have and have not given birth ≥ 10 months after diagnosis

	Women w/ birth ≥ 10 months after diagnosis			
	women w/ birth (cases) n=90		women w/o birth (matched controls) n=577	
	n	%	n	%
age at diagnosis				
<25	5	5.6	7	1.2
25-29	30	33.3	88	15.3
30-34	34	37.8	233	40.4
35-39	17	18.9	201	34.8
40-44	4	4.4	48	8.3
diagnosis year				
80-84	28	31.1	179	31.0
85-89	42	46.7	243	42.1
90-94	20	22.2	155	26.9
stage				
local	58	64.4	390	67.6
regional	29	32.2	184	31.9
distant	1	1.1	1	0.2
unknown	2	2.2	2	0.4
race				
white	61	67.8	405	70.2
black	29	32.2	172	29.8
Asian	0	0.0	0	0.0
other	0	0.0	0	0.0
unknown	0	0.0	0	0.0
multiple primaries				
none or after dx and after cases' birth	89	98.9	575	99.7
before birth and before dx	1	1.1	2	0.4
after dx but before cases' birth	0	0.0	0	0.0
vital status at follow up				
alive	73	81.1	419	72.6
dead	17	18.9	158	27.4

Table 3c. Characteristics of women in the Los Angeles area with primary breast cancer diagnosed 1980-93 who have and have not given birth ≥ 10 months after diagnosis

	Women w/ birth ≥ 10 months after diagnosis			
	women w/ birth (cases) n=171		women w/o birth (matched controls) n=1174	
	n	%	n	%
age at diagnosis				
<25	4	2.3	7	0.6
25-29	45	26.3	142	12.1
30-34	82	48.0	595	50.7
35-39	36	21.1	387	33.0
40-44	4	2.3	43	3.7
diagnosis year				
80-84	68	39.8	537	45.7
85-89	83	48.5	477	40.6
90-94	20	11.7	160	13.6
stage				
local	104	60.8	724	61.7
regional	56	32.8	413	35.2
distant	1	0.6	1	0.1
unknown	10	5.9	36	3.1
race				
white	116	67.8	988	84.2
black	24	14.0	101	8.6
Asian	14	8.2	28	2.4
other	11	6.4	39	3.3
unknown	6	3.5	18	1.5
multiple primaries				
none or after dx and after cases' birth	167	97.7	1148	97.8
before birth and before dx	0	0.0	0	0.0
after dx but before cases' birth	4	2.3	26	2.2
vital status at follow up				
alive	133	77.8	859	73.2
dead	38	22.2	315	26.8

Table 3d. Characteristics of women with primary breast cancer diagnosed 1980-93 who have and have not given birth ≥ 10 months after diagnosis (all study regions)

	Women w/ birth ≥ 10 months after diagnosis			
	women w/ birth (cases) n=343		women w/o birth (matched controls) n=2295	
	n	%	n	%
region				
Seattle	82	23.9	544	23.7
Detroit	90	26.2	577	25.1
Los Angeles	171	50.0	1174	51.2
age at diagnosis				
<25	12	3.5	17	0.7
25-29	99	28.9	288	12.6
30-34	154	44.9	1114	48.5
35-39	68	19.8	759	33.1
40-44	10	2.9	117	2295
diagnosis year				
80-84	122	35.6	880	38.3
85-89	162	47.2	960	41.8
90-94	59	17.2	455	19.8
stage				
local	217	63.3	1471	64.1
regional	111	32.4	782	34.1
distant	2	0.6	2	0.1
unknown	13	3.8	40	1.7
race				
white	253	73.8	1924	83.8
black	57	16.6	283	12.3
Asian	16	4.7	31	1.4
other	11	3.2	39	1.7
unknown	6	1.8	18	0.8
multiple primaries				
none or after dx and after cases' birth	337	98.3	2264	98.7
before birth and before dx	1	0.3	2	0.1
after dx but before cases' birth	5	1.5	29	1.3
vital status at follow up				
alive	276	80.5	1699	74.0
dead	67	19.5	596	26.0

Table 4. Duration of follow-up for women with primary breast cancer known to be alive in each region, by whether or not they had given birth ≥ 10 months after diagnosis.

Months since diagnosis	Seattle				Detroit				Los Angeles			
	women w/ birth		women w/o birth		women w/ birth		women w/o birth		women w/ birth		women w/o birth	
	n	%	n	%	n	%	n	%	n	%	n	%
0	2	2.9	1	0.2	0	0.0	2	0.5	1	0.8	42	4.9
1-24	0	0.0	7	1.7	0	0.0	11	2.6	1	0.8	12	1.4
25-36	0	0.0	3	0.7	1	1.4	14	3.3	0	0.0	6	0.7
37-48	4	5.7	17	4.0	2	2.7	23	5.5	3	2.3	22	2.6
49-60	2	2.9	33	7.8	5	6.9	38	9.1	0	0.0	30	3.5
61-72	5	7.1	36	8.6	10	13.7	45	10.7	8	6.0	39	4.5
73-84	5	7.1	38	9.0	6	8.2	38	9.1	13	9.8	56	6.5
≥ 85	52	74.3	286	67.9	49	67.1	248	59.2	107	80.5	652	75.9

Figure 1. Elapsed time from breast cancer diagnosis until live birth for women who gave birth <10 months after diagnosis (n=109)

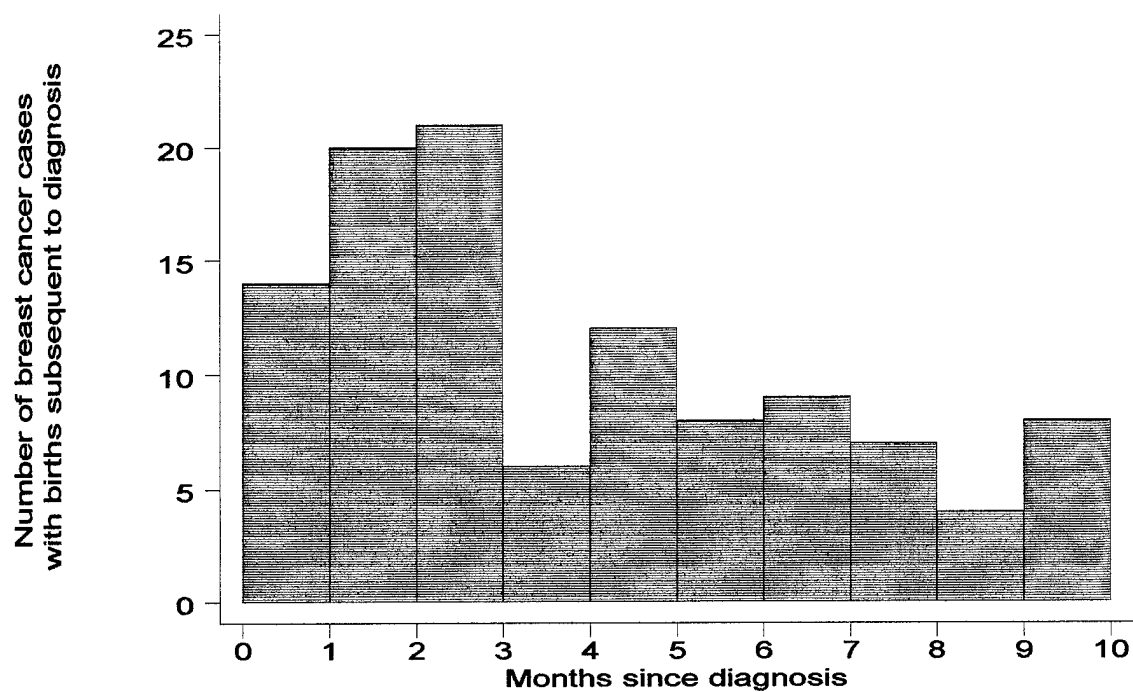
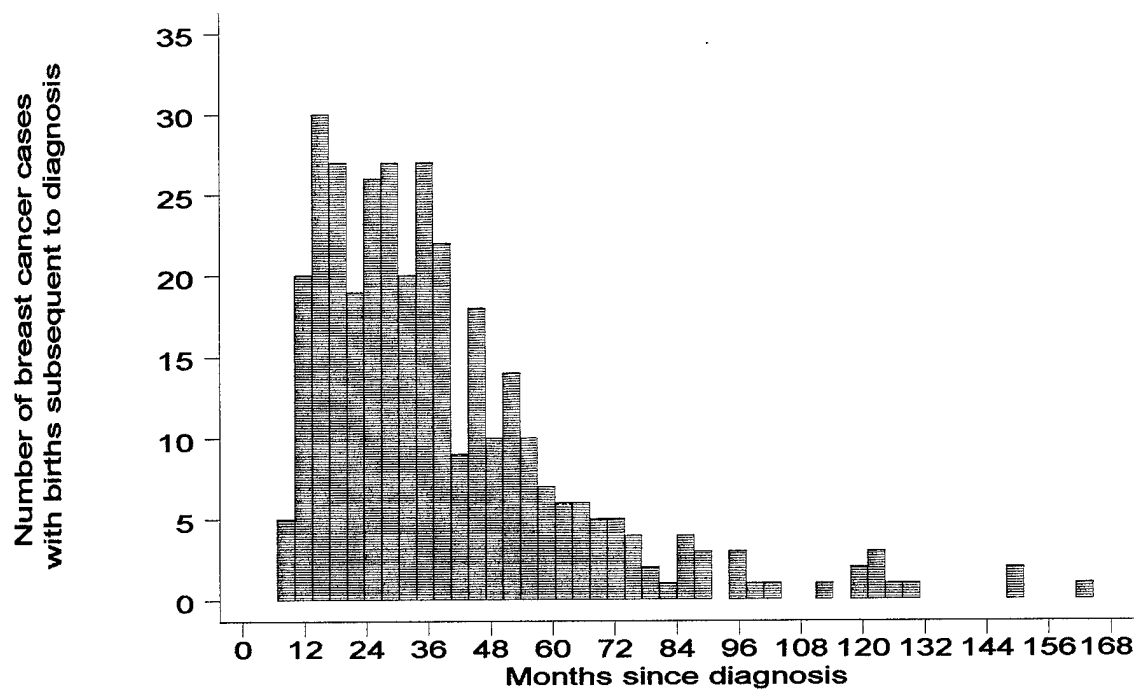


Figure 2. Elapsed time from breast cancer diagnosis until live birth for women who gave birth ≥ 10 months after diagnosis (n=343)



REFERENCES

1. Anderson BO, Petrek JA, Byrd DR, Senie RT, Borgen PI. Pregnancy influences breast cancer stage at diagnosis in women 30 years of age and younger. *Ann Surg Onc* 1996; 3(2): 204-11.
2. Bonnier P, Romain S, Dilhuydy JM, Bonichon F, Julien JP, Charpin C, et al. Influence of pregnancy on the outcome of breast cancer: a case-control study. *Societe Francaise de Senologie et de Pathologie Mammaire Study Group. Int J Cancer* 1997; 72(5): 720-7.
3. Collichio FA, Agnello R, Staltzer J. Pregnancy after breast cancer: from psychosocial issues through conception. *Oncology* 1998; 12(5): 759-65.
4. Kroman N, Jensen MB, Melbye M, Wohlfahrt J, Mouridsen HT. Should women be advised against pregnancy after breast-cancer treatment? *Lancet* 1997; 350(9074): 319-22.
5. Lethaby AE, O'Neill MA, Mason BH, Holdaway IM, Harvey VJ. Overall survival from breast cancer in women pregnant or lactating at or after diagnosis. *Auckland Breast Cancer Study Group. Int J Cancer* 1996; 67(6): 751-5.
6. Malone KE, Daling JR, Weiss NS, McKnight B, White E, Voigt LF. Family history and survival of young women with invasive breast carcinoma. *Cancer* 1996; 78: 1417-25.
7. Ranstam J, Janzon L, Olsson H. Rising incidence of breast cancer among young women in Sweden. *Br J Cancer* 1990; 61(1): 120-2.
8. Saunders CM, Baum M. Breast cancer and pregnancy: a review. *J Royal Soc Med* 1993; 86(3): 162-5.
9. vanderVange N, vanDongen JA. Breast cancer and pregnancy. *Eur J Surg Oncol* 1991; 17(1): 1-8.
10. White E, Daling JR, Norsted TL, Chu J. Rising incidence of breast cancer among young women in Washington State. *J Natl Cancer Inst* 1987; 79(2): 239-43